Health Alert: Syphilis
St. Louis Area

January 27, 2005

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Health Alert
January 27, 2005

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SUBJECT: **Syphilis Alert in the St. Louis Area**

The Missouri Department of Health and Senior Services (DHSS) alerts St. Louis area health care providers to an increase in syphilis among men who have sex with men (MSM), more than half of them being co-infected with HIV. This trend began in late fall of 2003, continued through 2004, and now it is very obvious that it is still on the rise within this population. The provisional data reflect that in 2004, there were 65 early syphilis[1] cases reported in St. Louis, of which 56 were males, and of those 56, 34 were self-identified MSM. Seventeen of the 65 cases were co-infected with HIV.

In the first three weeks of 2005, there have been at least 25 reactive syphilis blood tests with high titers from patients in the St. Louis area alone. Of the 25, five have been ruled out as previously treated cases. Of the remaining 20, DHSS Disease Intervention Specialists (DIS) have interviewed 11. Of the 11, ten are male; five self-identified as MSM (others suspected); and five are co-infected with HIV. Nine reactive reports are still pending investigation at the release of this alert.

Because effective treatment is available, it is important that persons whose sexual behaviors put them at higher risk for STDs be screened for syphilis every six months. Risks include, but not limited to, multiple sex partners, new sex partner, trading sex for money and/or drugs, anonymous sex, or having a sex partner that engages in high risk behaviors.

Syphilis is a sexually transmitted disease (STD) caused by the bacterium *Treponema pallidum*. It has often been called “the great imitator” because so many of the signs and symptoms of syphilis are similar to those of other diseases.

Syphilis is passed from person to person through direct contact with a syphilis lesion. Lesions occur mainly on the genitals, vagina, anus, or in the rectum. Lesions also can occur on the lips and in the mouth. Transmission of the organism occurs during vaginal, anal, or oral sex. Pregnant women with the disease can pass it to the babies they are carrying. Syphilis cannot be spread through contact with toilet seats, swimming pools, hot tubs, bath tubs, shared clothing, or eating utensils.

Genital lesions (chancres) caused by syphilis make it easier to transmit and acquire HIV infection sexually. There is an estimated two- to five-fold increased risk of acquiring HIV infection when syphilis is present. Ulcerative STDs, like syphilis, that cause lesions, ulcers, or breaks in the skin or mucous membranes, disrupt barriers that provide protection against infections.

1 Early syphilis includes all cases under one year’s duration, including primary, secondary, and early latent.

Clinical Manifestations

Although transmission appears to occur from persons with lesions who are in the primary or secondary stage, many of these lesions are unrecognized. Thus, most transmission is from persons who are unaware of their infection.

Primary Stage

The primary stage of syphilis is usually marked by the appearance of a single lesion (called a chancre), but there may be multiple lesions. The time between infection with syphilis and the start of the first symptom can range from 10 to 90 days (average 21 days). The chancre is usually firm, round, small, and painless. It appears at the spot where syphilis entered the body. The chancre lasts 3 to 6 weeks, and it heals without treatment. However, if adequate treatment is not administered, the infection progresses to the secondary stage.

Secondary Stage

Skin rash and mucous membrane lesions characterize the secondary stage. This stage typically starts with the development of a rash on one or more areas of the body. The rash usually does not cause itching. Rashes associated with secondary syphilis can appear as the chancre is healing or several weeks after the chancre has healed. The characteristic rash of secondary syphilis may appear as rough, red, or reddish brown spots both on the palms of the hands and the bottoms of the feet. However, rashes with a different appearance may occur on other parts of the body, sometimes resembling rashes caused by other diseases. Sometimes rashes associated with secondary syphilis are so faint that they are not noticed. In addition to rashes, symptoms of secondary syphilis may include fever, swollen lymph glands, sore throat, patchy hair loss, headaches, weight loss, muscle aches, and fatigue. The signs and symptoms of secondary syphilis will resolve with or without treatment, but without treatment, the infection will progress to the latent and late stages of disease.

Latent/Late Stages

The latent (hidden) stage of syphilis begins when secondary symptoms disappear. Without treatment, the infected person will continue to have syphilis even though there are no signs or symptoms; infection remains in the body. In the late stages of syphilis (over one year duration), it may subsequently damage the internal organs, including the brain, nerves, eyes, heart, blood vessels, liver, bones, and joints. This internal damage may show up many years later. Signs and symptoms of the late stage of syphilis include difficulty coordinating muscle movements, paralysis, numbness, gradual blindness, and dementia. This damage may be serious enough to cause death.

Diagnostic Considerations and Use of Serologic Tests

Darkfield examinations and direct fluorescent antibody tests of lesion exudate or tissue are the definitive methods for diagnosing early syphilis. A presumptive diagnosis is possible with the use of two types of serologic tests for syphilis: a) nontreponemal tests (e.g., Venereal Disease Research Laboratory [VDRL] and Rapid Plasma Reagin [RPR]) and b) treponemal tests (e.g., fluorescent

treponemal antibody absorbed [FTA-ABS] and *T. pallidum* particle agglutination [TP-PA]). The use of only one type of serologic test is insufficient for diagnosis, because false-positive nontreponemal test results may occur secondary to various medical conditions.

Nontreponemal test antibody titers usually correlate with disease activity, and results should be reported quantitatively. A fourfold change in titer, equivalent to a change of two dilutions (e.g., from 1:16 to 1:4 or from 1:8 to 1:32), is considered necessary to demonstrate a clinically significant difference between two nontreponemal test results that were obtained using the same serologic test. Sequential serologic tests in individual patients should be performed by using the same testing method (e.g., VDRL or RPR), preferably by the same laboratory. The VDRL and RPR are equally valid assays, but quantitative results from the two tests cannot be compared directly because RPR titers often are slightly higher than VDRL titers. Nontreponemal tests usually become nonreactive with time after treatment; however, in some patients, nontreponemal antibodies can persist at a low titer for a long period of time, sometimes for the life of the patient. This response is referred to as the "serofast reaction."

Most patients who have reactive treponemal tests will have reactive tests for the remainder of their lives, regardless of treatment or disease activity. However, 15%-25% of patients treated during the primary stage revert to being serologically nonreactive after 2-3 years. Treponemal test antibody titers correlate poorly with disease activity and should not be used to assess treatment response.

No test can be used alone to diagnose neurosyphilis. The VDRL-CSF is highly specific, but it is insensitive. Most other tests are both insensitive and nonspecific and must be interpreted in relation to other test results and the clinical assessment. Therefore, the diagnosis of neurosyphilis usually depends on various combinations of reactive serologic test results, abnormalities of cerebrospinal fluid (CSF) cell count or protein, or a reactive VDRL-CSF with or without clinical manifestations. The CSF leukocyte count usually is elevated (>5 WBCs/mm^3) in patients with neurosyphilis; this count also is a sensitive measure of the effectiveness of therapy. The VDRL-CSF is the standard serologic test for CSF, and when reactive in the absence of substantial contamination of CSF with blood, it is considered diagnostic of neurosyphilis. However, the VDRL-CSF may be nonreactive when neurosyphilis is present. Some specialists recommend performing an FTA-ABS test on CSF. The CSF FTA-ABS is less specific (i.e., yields more false-positive results) for neurosyphilis than the VDRL-CSF, but the test is highly sensitive. Therefore, some specialists believe that a negative CSF FTA-ABS test excludes neurosyphilis.

Diagnostic Considerations for HIV Infected Persons

Unusual serologic responses have been observed among HIV-infected persons who have syphilis. Most reports have involved serologic titers that were higher than expected, but false-negative serologic test results and delayed appearance of seroreactivity also have been reported. However, aberrant serologic responses are uncommon, and most specialists believe that both treponemal and non-treponemal serologic tests for syphilis can be interpreted in the usual manner for most patients who are co-infected with *T. pallidum* and HIV.

When clinical findings are suggestive of syphilis, but serologic tests are nonreactive or the interpretation is unclear, alternative tests (e.g., biopsy of a lesion, darkfield examination, or direct fluorescent antibody staining of lesion material) may be useful for diagnosis.

Neurosyphilis should be considered in the differential diagnosis of neurologic disease in HIV-infected persons.

Call the Department's Disease Investigation Unit at (573) 751-6113 for additional information or see the following websites:

http://www.cdc.gov/STD/treatment/

http://www.dhss.mo.gov/CDManual/Syphilis.pdf

Treatment

Penicillin G, administered parenterally, is the preferred drug for treatment of all stages of syphilis. The preparation(s) used (i.e., benzathine, aqueous procaine, or aqueous crystalline), the dosage, and the length of treatment depend on the stage and clinical manifestations of disease. However, neither combinations of benzathine penicillin and procaine penicillin nor oral penicillin preparations are considered appropriate for the treatment of syphilis.

The efficacy of penicillin for the treatment of syphilis was well established through clinical experience before the value of randomized controlled clinical trials was recognized. Therefore, almost all the recommendations for the treatment of syphilis are based on the opinions of persons knowledgeable about STDs and are reinforced by case series, clinical trials, and 50 years of clinical experience.

Parenteral penicillin G is the only therapy with documented efficacy for syphilis during pregnancy. Pregnant women with syphilis in any stage who report penicillin allergy should be desensitized and treated with penicillin. Skin testing for penicillin allergy may be useful in pregnant women; such testing also is useful in others.

The Jarisch-Herxheimer reaction is an acute febrile reaction frequently accompanied by headache, myalgia, and other symptoms that usually occurs within the first 24 hours after any therapy for syphilis. Patients should be informed about this possible adverse reaction. The Jarisch-Herxheimer reaction occurs most often among patients who have early syphilis. Antipyretics may be used, but they have not been proven to prevent this reaction. The Jarisch-Herxheimer reaction may induce early labor or cause fetal distress in pregnant women. This concern should not prevent or delay therapy.

2.4 million units IM in a single dose of Long-acting (LA) benzathine penicillin G is recommended for patients with an infection of less than one year's duration. Additional treatment is required for those infected longer. Complete detailed treatment guidelines can be found at: http://www.cdc.gov/STD/treatment/ .

Treatment for Those Co-infected with HIV

Compared with HIV-negative patients, HIV-positive patients who have early syphilis may be at increased risk for neurologic complications and may have higher rates of treatment failure with currently recommended regimens. The magnitude of these risks, although not defined precisely, is

likely minimal. No treatment regimens for syphilis have been demonstrated to be more effective in preventing neurosyphilis in HIV-infected patients than the syphilis regimens recommended for HIV-negative patients.

Management of Sex Partners

Sexual transmission of *T. pallidum* occurs only when mucocutaneous syphilitic lesions are present; such manifestations are uncommon after the first year of infection. However, persons exposed sexually to a patient who has syphilis in any stage should be evaluated clinically and serologically according to the following recommendations.

- Persons who were exposed within the 90 days preceding the diagnosis of early syphilis (i.e. primary, secondary, or early latent syphilis) in a sex partner might be infected even if seronegative; therefore, such persons should be treated presumptively with 2.4 million units of Benzathine Penicillin G LA.
- Persons who were exposed >90 days before the diagnosis of primary, secondary, or early latent syphilis in a sex partner should be treated presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain.
- For purposes of partner notification and presumptive treatment of exposed sex partners, patients with syphilis of unknown duration who have high nontreponemal serologic test titers (i.e., ≥1:32) can be assumed to have early syphilis. However, serologic titers should not be used to differentiate early from late latent syphilis for the purpose of determining treatment.
- Long-term sex partners of patients who have latent syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of the evaluation findings.

For identification of at-risk partners, the time periods before treatment are: a) 3 months plus duration of symptoms for primary syphilis; b) 6 months plus duration of symptoms for secondary syphilis; and c) 1 year for early latent syphilis.

DHSS's STD Disease Intervention Specialists (DIS) will provide assistance in confidential partner elicitation, notification, and referral for appropriate evaluation and treatment. Call the Section for Communicable Disease Prevention to identify your local STD DIS at (573) 751-6113.

Reporting

Missouri law requires health care providers and laboratories to report all reactive syphilis test results and diagnoses within 24 hours, preferably immediately by telephone to (573) 751-6113. The complete rule, 19 CSR 20-20.020 can be found at:

http://www.sos.mo.gov/adrules/csr/current/19csr/19c20-20.pdf .

Health care providers are also requested to assist in the control of syphilis through immediate reporting of suspect cases by telephone to the DHSS Section for Communicable Disease Prevention at (573) 751-6113, or 24/7 to (800) 392-0272. Disease case reports (using a CD-1 form) can be faxed to (573) 526-0235.

References

Centers for Disease Control and Prevention, Division of Sexually Transmitted Diseases. STD Facts and Information-Syphilis.
http://www.cdc.gov/nchstp/dstd/SyphilisInfo.htm

Centers for Disease Control and Prevention, Division of Sexually Transmitted Diseases. 2002 STD Treatment Guidelines
http://www.cdc.gov/STD/treatment/

Missouri Department of Health and Senior Services, Section for Communicable Disease Prevention. Communicable Disease Investigation Reference Manual
http://www.dhss.mo.gov/CDManual/CDManual.htm